#### REMARKS

Reconsideration of the application, as amended, is respectfully requested.

#### Status of the claims

The applicants and undersigned representative wish to thank the Examiner for the interview on March 15, 2005 to discuss the claims and proposed amendments for this application. Claims 37-72 were pending in this application. Claims 37, 41, 43, 45, 48, 50, 52, 55, 64, 69 were amended and new claims 73-84 were added to further clarify the invention. Support for the amendment of the claims can be found in the specification as filed. See, for instance, page 8, line 31 to page 9, line 5 and page 13, line 5-14. Support for the new claims can be found in the specification as filed. See, for instance, page 4, line 21 to page 8, line 3. Accordingly, no new matter has been introduced into this application as a result of the present amendment.

#### **Claim interpretation**

The Examiner interprets nanoparticles as a particle of any size, absent an express definition in the specification. Contrary to the Examiner's position, the Applicants respectfully submit that an ordinary skilled artisan would understand from the teachings of the specification that nanoparticles refers to particles in the nanometer range. See, for instance, the specification at page 8,line 31 to page 9, line 5. For instance, U.S.S.N. 09/760,500 (now Applicant's U.S. Patent no. 6,767,702), recites suitable nanoparticles having a size ranging from 5 to about 150 nm (mean diameter) See, for instance, the original claims and the specification at pages 8, line 31 to page 9, line 5. See also the specification at page 10, line 29; page 11, line 2; page 12, line 28; and page 13, line 18. The claims were amended to include size ranges and thus the Examiner's interpretation is without basis.

#### Claim Rejections under 35 USC § 102(b) and (e) based on Abbott

Claims 3 37, 38, 40, 42, 45, and 55-60 stand rejected under 35 U.S.C. § 102(b), alleged to be anticipated by Abbott et al. (U.S. Patent 6,277,489)("Abbott"). Claims 37-40, 43, 46-51 and 72 were also rejected under 35 U.S.C. § 102(b), alleged to be anticipated by Abbott. The Examiner alleged that the present invention is old because Abbott allegedly

taught a multilayered material comprising a particulate substrate, a metal film layered onto the substrate, and a recognition moiety attached to the metal layer. Further, the particulate substrate is alleged to be any size. With respect to claims 47-51 and 72, the Examiner alleged that it is unclear how making the product of these claims makes the claimed composition different from Abbott's product. On this basis, the Examiner believes that Abbott anticipates the claimed invention. The Applicants respectfully traverse the rejection.

As a general rule, for prior art to anticipate under section 102, every element of the claimed invention must be identically disclosed in a single reference. Corning Glass Works v. Sumitomo Electric, 9 U.S.P.Q.2d 1962, 1965 (Fed. Cir. 1989). The exclusion of a claimed element, no matter how insubstantial or obvious, from a reference is enough to negate anticipation. Connell v. Sears, Roebuck & Co., 220 U.S.P.Q 193, 1098 (Fed. Cir. 1983). Applicants respectfully submit that none of the references cited against the pending claims can applied to support an anticipation rejection of the claims under 35 U.S.C. sections 102 (b) and (e).

Abbott fails to teach the elements of the instant invention as presently claimed. Abbott merely relates to a multilayered material of particulate substrate, a metal film layered onto the substrate, and a recognition moiety e.g., biomolecules, attached to the metal layer. Abbott merely deals with conventional coating methods as discussed in col. 11, lines 51-55; col. 37, lines 24-32; col. 55, lines 59-66. Specifically, Abbott is directed to micrometer sized silica cores having multilayered metal coatings. Indeed, all of his examples teach preparation of microsized silica-core multilayered products, not nanoparticle conjugates of the size range recited in the present claims, e.g., instant claim 37. See col. 55, line 20 to col. 61, line 33. Furthermore, Abbott does not disclose or suggest "core/shell nanoparticles oligonucleotide conjugates," and further having a "gold shell of a predetermined thickness" and a "core/shell nanoparticle having a mean diameter ranging from 5 to 150 nm" (instant claim 37), a method for making such nanoparticle conjugates (instant claim 55), and a method for using such nanoparticle conjugates for detecting nucleic acids (instant claim 69).

With respect to claims 47-51 and 72, the product produced by the recited process is different from Abbott's product. For instance, Abbott's product is produced by treating silica gel with a pre-made conventional solution of a gold salt and a reducing agent. See

col. 55, lines 59-66. This conventional process results in the undesirable production of gold aggregates as a competing side reaction during the plating process due to the formation of gold cluster nucleation sites. Evidence of aggregate production in Abbott's product can be found in Abbott at col. 56, lines 25-28. In contrast, the simultaneous dropwise addition of the gold salt and reducing agent by the inventive process inhibits formation of these nucleation sites. See the specification, for instance, at page 13, lines 12-14. Thus, the products produced by the presently recited process and Abbott's process are not the same.

Accordingly, Abbott cannot be said to anticipate the presently claimed invention. Withdrawal of the section 102(b) and (e) rejections of the claims based on Abbott is in order and is respectfully requested.

## Claim Rejection under 35 USC § 103 based on Abbott in view of Mirkin

Claims 41, 44, 45, and 69-71 stand rejected under 35 U.S.C. § 103(a), alleged as unpatentable over Abbott (cited above) in view of Mirkin et al. (US 6,361,944)("Mirkin"). More specifically, Abbott is re-alleged as above while Mirkin is alleged to teach nanoparticle-oligonucleotide conjugates used in detection of nucleic acids, wherein the nanoparticles are magnetic, including cores of Fe<sub>3</sub>O<sub>4</sub> with a silica shell, conjugated to oligonucleotides. Mirkin is further alleged to teach nanoparticle-oligonucleotide conjugates in hybridization methods, including methods for detection on a surface. The Examiner asserts that it would be obvious to an ordinary skilled artisan to use the magnetic core of Mirkin in the particles of Abbott, motivated by the desire for easy separation of magnetic particles having hybridized targets from a test solution. Applicants respectfully traverse the rejection.

The Federal Circuit reiterated the manner in which obviousness rejections are to be reviewed. Where claimed subject matter has been rejected as obvious in view of a combination of prior art references, "a proper analysis under § 103 requires, *inter alia*, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success." *In re Vaeck*, 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991),

citing *In re Dow Chemical Co.*, 837 F.2d 469, 473, 5 U.S.P.Q. 2d 1529, 1531 (Fed. Cir. 1988). Applicants respectfully submit that the combination of Abbott and Mirkin does not teach or suggest the Applicants' invention as presently claimed.

The presently claimed invention relates to core/shell nanoparticle conjugates having (a) a magnetic core and a non-alloying gold shell surrounding the core and (b) oligonucleotides bound to the gold shell (see, e.g., claim 37); a method for preparing such conjugates (see, e.g., claim 55) and methods for using the conjugates (see, e.g., claim 69). The core/shell nanoparticles prepared by a recited process which inhibits the formation of gold cluster nucleation sites, thus avoiding side reactions leading to gold aggregate formation as seen in Abbott's process for making microparticles and depletion of available gold from the reaction mixture. Neither Abbott nor Mirkin teach or suggest the Applicant's process for making core/shell nanoparticles by the recited process as presently claimed or even suggest that this would be even possible or desirable to do. Accordingly, Applicants respectfully submit that withdrawal of the rejection of the claims under 35 U.S.C. § 103(a) based on the combination of Abbott with Mirkin is in order and is respectfully requested..

## Provisional Double Patenting rejection (same invention)

The Examiner rejected claims 37-51 of the present application under 35 U.S.C. 101 for double patenting in view of claims 40-47 and 50-55 of co-pending application serial no. 10/153,483 and claims 3-10 of co-pending application serial no. 10/397,579. The Applicants request that the Examiner hold this provisional rejection in abeyance until the claims in this application or either of the co-pending application have been found to be allowable.

## Provisional Double Patenting rejection (obviousness-type)

The Examiner rejected claims 69-71 of the present application under 35 U.S.C. 103 for obviousness-type double patenting in view of claims 32-34 of co-pending application serial no. 10/397,579. The Applicants request that the Examiner hold this rejection in abeyance until the claims in this application or either of the co-pending application have been found to be allowable.

# **Conclusion**

In light of the above arguments, the Examiner is respectfully requested to reconsider the application as claimed. If the Examiner believes that a telephonic or personal interview would expedite prosecution of the application, she is invited to contact the undersigned at (312) 913-0001.

Date: June 21, 2005

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